


APPLICANTS: Comb *et al*
U.S.S.N.: 09/535,364

Amendments to Specification

Kindly replace the existing "Abstract", on pages 59-60 of the specification, with the following amended paragraph (indicating changes made):

-- ~~A method is provided for producing motif specific, context independent antibodies which are specific to at least one fixed amino acid residue, whether modified or unmodified, in the context of variable surrounding amino acid or peptide sequences. The method includes the steps of (1) constructing a peptide library featuring at least one fixed amino acid and variable surrounding amino acids, and (2) immunizing a host with this peptide library. Antibodies may optionally be isolated and purified from the antisera of this immunized host. The disclosed method encompasses both modified motifs, such as phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine, as well as unmodified motifs.~~

 Also provided are A class of motif-specific, context-independent antibodies that bind conserved signal transduction motifs, such as kinase consensus substrate motifs and protein-protein binding motifs, containing one or more modified amino acids, such as a phosphorylated amino acid, is provided. The antibodies bind a plurality of peptides or proteins that contain the modified motif. Context-independent antibodies specific for single modified residues, such as phosphothreonine, are also provided, specific for at least one fixed amino acid in the context of variable surrounding peptide sequences, including phosphothreonine, phosphoserine, MAPK substrate consensus sites, 14-3-3 consensus binding sites, CDK substrate consensus sites, PKA substrate consensus sites, Akt substrate consensus sites and acetylated lysine, and other modified and unmodified amino acids as such fixed residues. Methods for producing and using such antibodies are provided.

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~~Methods for utilizing such antibodies to screen for unknown substrates of modification enzymes, enzymatic modification of substrates, including drug screens, and to identify enzymes which modify a given substrate are also provided.~~

~~Also provided are methods for profiling protein levels and post-translational modifications, including changes resulting from drug treatment, on a genomic scale by utilizing motif specific, context independent antibodies directed to conserved motifs on large and diverse protein populations. --~~

Also kindly replace the existing paragraph on page 34, lines 19-27, of the specification, with the following amended paragraph (indicating changes made):

✓ Results confirmed that the phosphothreonine antibodies tolerated all amino acids in the -1, -2, -3, -4, and +2, +3 position, and bound equally well to every amino acid except proline at the +1 position (see Figure 1d, first row). The reactivity as defined by this binding profile indicates that the antibodies will bind all phosphothreonine containing sequences except those followed immediately in [-1] +1 position by proline. Further analysis using a variety of specific phosphothreonine containing peptides confirmed these results. ✓